

IN THE SPECIFICATION:

Please amend the first full paragraph on page 2 as follows:

Cross Reference Cross-Reference to Related Application: This application is a divisional of application Serial No. 09/177,814, filed October 23, 1998, pending.

Please amend the paragraph bridging pages 5 and 6 as follows:

The use of substantially smooth, open-channeled capillary columns in miniature chromatographs is, however, somewhat undesirable from the standpoint that ~~open-channeled~~ open ~~open-channeled~~ columns typically have a surface area that is limited by the area of the substantially smooth surface of the channel. The amount of stationary phase material that may be disposed along a given length of substantially smooth, open-channeled capillary columns is also limited by the surface area of that length of the capillary column. Thus, in order to effectively separate the various constituents of a sample, the capillary column must be relatively long. Consequently, the substrate on which the capillary column is formed must have a sufficient surface area to facilitate fabricating the capillary column thereon. Thus, the use of substantially smooth, open-channeled capillary columns in miniature gas chromatographs imposes minimum size limitations on such chromatographs.

Please amend the second full paragraph on page 7 as follows:

The sample separation apparatus of the present invention includes a substrate with a capillary column thereon, the latter comprising a rough surface, such as a matrix which defines a plurality of pores therethrough or an open column with a rough surface, which is also referred to as a matrix. The surface area of the matrix of each capillary column facilitates the separation of the constituents of a sample over a relatively short length of the column compared to the required lengths of conventional smooth, ~~“open”~~, “open,” etched or ablated columns to effectively separate the constituents. Preferably, the capillary column, which is also referred to as a porous capillary column, comprises porous silicon or hemispherical grain silicon, and is formed on a silicon substrate. Such a column, depending on the width and depth thereof, may be useful for

separating the constituents of a sample or detecting constituents in a sample having a volume of as small as about one femtoliter (1×10^{-15} liter). The separation apparatus may also include a detector disposed proximate the capillary column. Such a detector analyzes a characteristic of a constituent as the constituent passes through the capillary column, and thereby identifies or otherwise analyzes the constituent.

Please amend the ninth full paragraph on page 10 as follows:

With reference to FIG. 1, a first embodiment of a sample separation apparatus 10 of the present invention is depicted. Sample separation apparatus 10 includes a substrate 12 and capillary columns 14 formed in the substrate. Capillary columns 14 each include a matrix 16 and a plurality of pores 18 formed through the matrix. Pores 18 permit gases and liquids to flow along the distance of capillary columns 14. Capillary columns 14 may also include one or more reaction regions 20 along the longitudinal extent thereof. Preferably, ~~each of~~ the reaction regions 20 along each capillary column 14 are discrete from one another. Sample separation apparatus 10 may also include one or more detectors 22 disposed proximate each capillary column 14.

Please amend the paragraph bridging pages 12 and 13 as follows:

Separation apparatus 10 may also include a processor 80 and a memory device 82, each of a type known in the art. Processor 80 receives information about sample 70, or “sample information,” information,” from one or more types of detectors 22 along column 14 and processes the sample information to output same in a user-friendly format to a display 84 external of sample separation apparatus 10. In processing the sample information, processor 80 may compare the sample information to known information that has been stored in memory device 82, and thereby identify the sample or generate other data regarding the sample information. The sample identity may then be transmitted to display 84. Following the comparison of sample information to known information, processor 80 may direct memory device 82 to store information about the sample, including its identity and associated data.

Please amend the first full paragraph on page 14 as follows:

Alternatively, as depicted in FIG. 2a, migration facilitator 24' may comprise a vacuum source 28', as known in the art, which exerts a negative pressure on sample ~~70~~ in 70' in order to pull the sample along each capillary column 14'. Such a vacuum source is operatively attached to capillary column 14', and in flow communication therewith, proximate an exit end 14b', or second end, thereof. Preferably, the amount of negative pressure that is generated by vacuum source 28' and applied to each capillary column 14' may be adjusted or varied.

Please amend the second full paragraph on page 14 as follows:

FIG. 3 illustrates a third embodiment of the sample separation apparatus 10" of the present invention, which is particularly useful for conducting electrophoretic separation on a sample 70". The degree to which the constituents of sample ~~70~~ are 70" are separated depends upon the cross-sectional diameter of pores 18". Accordingly, the greatest degree of separation occurs when the size of pores 18" is approximately equivalent to the size of the various constituents of sample 70" for which separation is desired, or the "targeted" constituents. Thus, pores 18" of small cross-sectional diameters separate the smaller constituents of sample 70". Pores 18" of larger ~~cross-~~ cross-~~sectional~~ cross-sectional diameters permit the migration and separation of the larger sized constituents through each capillary column 14". Thus, the cross-sectional diameter of pores 18" preferably facilitates separation of the various targeted constituents of sample 70".

Please amend the paragraph bridging pages 14 and 15 as follows:

Electrophoretic techniques typically employ an electric current to move the constituents of sample 70". Thus, sample separation apparatus 10" may include a migration facilitator ~~24"~~ ~~which~~ that comprises an electric current-generating component 30. Current-generating component 30 includes a first electrode 32 disposed proximate a sample application end 14a",

which is also referred to as a first end, of each capillary column 14", and a second electrode 34 that is positioned proximate exit end 14b" of each capillary column 14". First and second electrodes 32 and 34, respectively, are fabricated from an electrically conductive material, and are connectable to opposite electrical charges so as to facilitate the generation of a current along a length of the capillary column. Thus, first and second electrodes 32 and 34, respectively, facilitate the migration of the constituents of sample 70" along their respective capillary columns 14" and the separation of the constituents during migration.

Please amend the first full paragraph on page 17 as follows:

Alternatively, patterning may include a mask and etch, as known in the art, followed by damaging, or "~~roughing~~", "roughing," the exposed areas of substrate 12 to define capillary column regions 40, as disclosed in United States Patent 5,421,958 (the "'958 patent"), which issued to Robert W. Fathauer et al. on June 6, 1995, the disclosure of which is hereby incorporated by reference in its entirety. It is known in the art that porous silicon forms more readily on damaged, or roughened, areas on the surface of a silicon substrate 12. As the '958 patent discloses, the damaging of substrate 12, or the creation of imperfections on same, may include, without limitation, mechanically damaging substrate 12 and applying energetic beams to substrate 12.

Please amend the paragraph bridging pages 17 and 18 as follows:

FIG. 7 schematically illustrates an anodization chamber 50 in which an exemplary process for porifying capillary column regions 40 of substrate 12 (*see* FIG. 6) may occur. The porifying of capillary column regions 40 in order to define capillary columns 14 (*see* FIGs. 1 and 6) in substrate 12 may be performed by conventional processes, including processes for forming porous silicon regions in semiconductor devices. Exemplary process for forming porous silicon from a silicon substrate are disclosed in each of the '700, '759, and '958 patents. Such porification processes typically include positioning substrate 12 within an anodization chamber 50, adjacent a partition 52, which separates the anodization chamber into a first cell 54

and a second cell 55, which are also referred to as "sections". "sections." An anode 56 extends into first cell 54. Similarly, a cathode 57 extends into second cell 55. Partition 52 includes an opening 53 therethrough, which is covered by substrate 12 and sealed to prevent the passage of liquids between first cell 54 and second cell 55. Thus, an upper surface 12a of substrate 12 is exposed to first cell 54, while an opposing base surface 12b is exposed to second cell 55. First cell 54 is filled with an anodizing solution 58, such as concentrated hydrofluoric acid, while second cell 55 is filled with an electrically conductive liquid 59, such as 50% isopropyl alcohol. By means of anode 56 and cathode 57, an electric current is then applied to anodization chamber 50. As current passes through substrate 12, the areas of upper surface 12a that are exposed to first cell 54 become porous.

Please amend the paragraph bridging pages 18 and 19 as follows:

With reference to FIG. 8, as another alternative, capillary columns 214 that include hemispherical grain silicon 216 on the surfaces 215 thereof may be formed in selected regions of a substrate 212 by known techniques. First, an elongate trench 213, which defines the path of the capillary column, is defined in a substrate by known patterning processes, such as mask and etch techniques. The area of the surfaces of trench 213 may then be increased by known methods, such as by forming hemispherical grain ~~silicon~~ 215 silicon 216 thereon. Exemplary methods of forming hemispherical grain silicon that may be employed to fabricate capillary columns 214 include those disclosed in United States Patent 5,407,435, 5,407,534, which issued to Randhir P.S. Thakur on April 18, 1995; United States Patent 5,623,243, which issued to Hirohito Watanabe et al. on April 22, 1997; United States Patent 5,634,974, which issued to Ronald A. Weimer et al. on June 3, 1997; United States Patent 5,721,171, which issued to Er-Xuan Ping et al. on February 24, 1998; and United States Patent 5,726,085, which issued to Darius Lamont Crenshaw et al. on March 10, 1998, the disclosures of each of which are hereby incorporated by reference in their entirety. In general, a film of amorphous silicon is formed in trench 213. Impurities are then seeded into the amorphous silicon. Then, the material is annealed to cause nucleation sites to grow at the seeding sites to thereby form the rough textured hemispherical

grain silicon 216. A solid phase 218, such as a native oxide layer, may then be grown on the surface of the hemispherical grain silicon 216. Finally, the entire structure 210 may be enclosed by a cover layer 220 or a suitable package.

Please amend the second full paragraph on page 19 as follows:

Referring again to FIGs. 1-1b, detector 22, processor 80, memory device 82, valves 25, first electrode or cathode 32 (FIG. 3), or second electrode or anode 34 (FIG. 3) and other components that are carried upon substrate 12 may be fabricated upon the substrate in a desired location by known semiconductor fabrication processes. Such semiconductor fabrication processes include, without limitation, layer deposition processes (e.g., sputtering and chemical vapor deposition); oxidation processes; patterning processes (e.g., masking and etching); and other conventional semiconductor device fabrication processes.

Please amend the paragraph bridging pages 21 and 22 as follows:

As an example of the use of sample separation apparatus-110, 100, which is illustrated in FIG. 4, a constituent, or an “analyte” 172, of a sample 170 is isolated from the remainder of the sample. Sample 170 is applied to first end 114a of at least one capillary column 114. As sample 170 moves through column 114, each of the constituents of the sample, including analyte 172, contact capture substrate 117. If sample 170 includes any analytes 172 for which capture substrate 117 has an affinity, these analytes are bound by the capture substrate 117 and isolated from the remainder of the sample as the sample contacts and passes by the capture substrate. The presence or absence of capture substrate 117-bound analytes 172 may then be detected by detector 122, by staining, spectrophotometrically, radiographically, or by other detection or identification techniques that are known in the art. The concentration or relative amounts of each isolated analyte 172 may also be determined in such a manner.

Please amend the first full paragraph on page 22 as follows:

As another example of the use of sample separation apparatus-110-, 100, to detect the presence of silver, capillary column 114 may be provided with a free chloride source, such as calcium chloride or sodium chloride. When an aqueous solution containing silver is drawn into the capillary column 114, resultant precipitation of silver chloride would reduce the chloride concentration in capillary column 114. The resultant reduced ionic conductivity in capillary column 114 may be measured by detector 122 and compared to a conductivity profile stored in a memory element associated with sample separation apparatus-110-, 100. For the purpose of comparison, another capillary column 114' of sample separation apparatus-110-, 100 may be provided with no free chloride source. As the aqueous silver solution is drawn into the second capillary column 114', the ionic conductivity of the second capillary column 114' may be measured by another detector. The ionic conductivity profile of the second capillary column 114' may be compared to that of the first capillary column 114 and to the conductivity profile. The measured and stored data may then be processed to determine the concentration of silver in the original sample.